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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/681,205 | 10/09/2003 | Syozo Kobayashi | 243895US0DIV | 5872 |

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OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
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EXAMINER

TUCKER, ZACHARY C

ART UNIT PAPER NUMBER

1624

DATE MAILED: 06/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|--------------------------------------|---|--|
| Office Action Summary | Application No. 10/681,205 | Applicant(s) KOBAYASHI ET AL. | |
| | Examiner Zachary C. Tucker | Art Unit 1624 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 April 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11, 17 and 23-26 is/are pending in the application.
- 4a) Of the above claim(s) 3, 5-8 and 11 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4, 9, 10, 17 and 23-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☒ Certified copies of the priority documents have been received in Application No. 09/762,888.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____. | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____. 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) 6) <input type="checkbox"/> Other: _____. |
|--|--|

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after the Final Rejection letter mailed 29 September 2005 (hereinafter "previous Office action"). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 27 April 2006 has been entered.

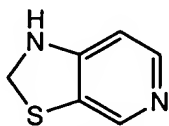
Response to Amendment

As requested in the 27th April 2006 correspondence accompanying the Request for Continued Examination (hereinafter "present amendment") claims 1, 2, 10 and 11 have been amended.

Election/Restrictions

The search of the instant claims was broadened in view of the present amendment. Art anticipating the invention was found, whereupon the search was stopped. Claims 3, 5-8, and 11, which do not read on the species elected for examination remain withdrawn from consideration. No claim in the application has been completely searched.

Note: "tetrahydrothiazolopyridyl," as recited in instant claim 11, describes a group of the structure:



, as opposed to the "4,5,6,7-tetrahydrothiazolo[5,4-c]pyridinyl" group of the compound of the elected species. "Tetrahydro," as recited in "tetrahydrothiazolo" in instant claim 11, since it appears immediately before "thiazolo," describes the *thiazole* ring, not the pyridine ring. In the more specific compound name in provided in Example B-54 of the specification, which is the elected species for examination, the *position numbers* of the hydrogenated bonds are provided, as opposed to the terminology of instant claim 11, which does not designate the position of the hydrogenated bonds. As such, it must be afforded the most reasonable interpretation, which is that the "tetrahydro" describes the ring which it immediately precedes, not the ring specified at the end of the term. Nothing in the specification sets forth a special definition of "tetrahydrothiazolo" which would require the term to be

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interpreted such that the "tetrahydro" is actually describing the pyridine ring, not the thiazole ring which it immediately precedes.

Status of Claim Rejections - 35 USC § 112

In the previous Office action, claims 1, 2, 4, 9, 10, 17 and 23-26 were finally rejected under the second paragraph of 35 U.S.C. 112, for indefiniteness of the term "substituted or unsubstituted," since no descriptor of what kinds of or how many substituents are provided in the claim, nor are any such descriptors concretely set out in the specification.

In view of the present amendment, which deletes the phrase "substituted or unsubstituted" in all occurrences, the rejection is hereby withdrawn.

Status of Claim Rejections - 35 USC § 102

In the previous Office action, claims 1, 9, 10 and 17 were finally rejected under 35 U.S.C. 102(b) as being anticipated by US 4,857,644 (Abou-Gharbia).

In view of the present amendment, the rejection is hereby withdrawn. Instant claim 1, and therefore all claims which depend from claim 1, now require that *both* Q¹ and Q^A are polycyclic, while compounds from Abou-Gharbia only include monocyclic substituents at the part of the molecule corresponding to Q¹ of the instant claims.

In the previous Office action, claims 1, 2, 4, 9, 10, 17, 23 and 24 were rejected under 35 U.S.C. 102(b) as being anticipated by WO 98/21188 (Preston et al).

In view of the present amendment, the rejection is hereby withdrawn. Instant claim 1, and therefore all claims which depend from claim 1, now require that *both* Q¹ and Q^A are polycyclic. Since Preston et al only provides for substituents at the position corresponding to Q¹ which are monocyclic, the reference no longer anticipates any of the instant claims.

Status of Claim Rejections - 35 USC § 103

In the previous Office action, claims 25 and 26 were held to be unpatentable under 35 U.S.C. 103(a) in view of WO 98/21188 (Preston et al).

Because the rejection under 35 U.S.C. 102 upon which the '103 rejection in view of Preston was based has been overcome by applicants' amendment, the rejection under '103 is no longer tenable and is therefore hereby withdrawn.

New Claim Rejections

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

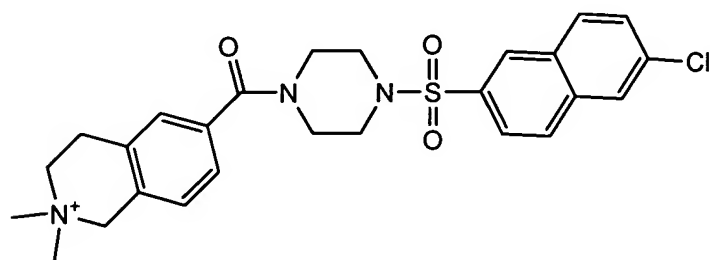
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-11, 17 and 23-26 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,525,042. Although the conflicting claims are not identical, they are not

patentably distinct from each other because the claims of the patent, when read in light of the specification, especially the examples, render the instant claims obvious. When considering the significance of the claims of a patent, it is proper to look to the disclosure as a dictionary to determine the meaning of broad concepts set forth in those claims, such as a claim drawn to a genus of chemical compounds. Claim 1 of US 6,525,042 is such a claim.

Example 116 of US 6,525,042 describes the compound 6-[[4-[(6-chloronaphthalen-2-yl)sulfonyl]piperazin-1-yl]carbonyl]-2,2-dimethyl-1,2,3,4-tetrahydroisoquinolinium iodide.



Claim 1 of the patent, of course, embraces this compound. Examples in a patent disclosure are a means of describing the most preferred embodiments of an invention, which is set out in the claims of the patent. In the case of patent US 6,525,042, the exemplified compounds are examples of embodiments of claim 1 therein. As such, one of ordinary skill in the art would find it obvious to make the compound according to Example 116 of US 6,525,042, in view of claim 1 of the patent. Therefore, claim 1 of US 6,525,042 renders instant claims 1-10, 17 and 23-26 obvious because the compound according to Example 116 of the patent is indeed a compound according to instant claims 1-10, 17 and 23-26. In other words, the choice of 2,2-dimethyl-1,2,3,4-tetrahydroisoquinolinium iodide for the "unsaturated bicyclic fused ring group" of Q¹, "a single bond" for Q², carbonyl for T¹ (T¹ is always carbonyl), 1,4-piperazinyl for Q³ (R⁸

and R⁹ are hydrogen, a and b are both zero, c is two), and 6-chloronaphthalen-2-yl for the group bonded to the right of the sulfonyl in the structure depicted in claim 1 of the patent (R¹ and R³ are coupled together to form an alkenylene group) would be obvious. As such, the choice of those identities from claim 1 of the patent renders instant claim 1 unpatentable under the doctrine of obviousness-type double patenting.

Instant claim 11 is obvious over the claims of the patent in view of tetrahydrothienopyridyl being recited as an alternative Q¹ group in claim 4 of the patent. So, replacing the 2,2-dimethylisouinolium iodide group of the compound according to example 116, which is pointed out *supra*, with said tetrahydrothienopyridyl group would be obvious in light of that identity being recited in claim 4.

Instant claims 3, 5, 6, 7 and 8 are included in this rejection because they further modify optional elements of the compounds according to instant claim 1.

Instant claim 4 requires R¹⁸ to be halogen or ethynyl. In the reference compound, the corresponding group is halogen (chloro), on the naphthalene ring system.

The pharmaceutical composition claims and method of use claims in the instant application and in the patent correspond in scope to one another in that if a compound according to claim 1 of both is obvious, then the composition and method of use is similarly obvious in light of the patented claims.

Claims 1-11, 17 and 23-26 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 6, 10 and 22-24 of U.S. Patent No. 6,747,023, which issued from the parent application to the instant application. Although the conflicting claims are not identical, they are not patentably distinct from each other because compounds according to claims 22-24 of the patent

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anticipate instant claims 1-10, the pharmaceutical composition according to claim 6 of the patent anticipates instant claim 17 and the method according to claim 10 of the patent anticipates instant claims 23-26. Because the compounds according to claims 22-24 are included in claim 1 of the patent, then the choice of those compounds as the active ingredient in the pharmaceutical composition claimed in that patent and as the therapeutic agent administered in the method of treatment claimed in that patent would be obvious to one of ordinary skill. Thus the instant claims cover subject matter already patented by applicants in US 6,747,023.

The compounds according to claims 22-24 of the patent anticipate instant claim 1-10 wherein Q¹ is a dicyclic fused ring group (tetrahydropyridothiomorpholine and pyridothiomorpholine); Q² is a single bond; T¹ is a carbonyl group; Q³ is piperazinyl; Q^A is an arylalkenyl group (phenylethylenyl).

Instant claims 3, 5, 6, 7 and 8 are included in this rejection because they further modify optional elements of the compounds according to instant claim 1.

Instant claim 4 requires R¹⁸ to be halogen or ethynyl. In the compounds according to claims 22-24 of the patent, the corresponding group is halogen (chloro), on the phenylethylenyl group.

Instant claim 11 is included in this rejection, because tetrahydrothienopyridyl is recited as one of the alternative identities of Q¹ in claim 4 of the patent. As such, replacement of the pyridothiomorpholine groups with tetrahydrothienopyridyl as Q¹, as recited in instant claim 11, would be obvious in light of claim 4 of the patent.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

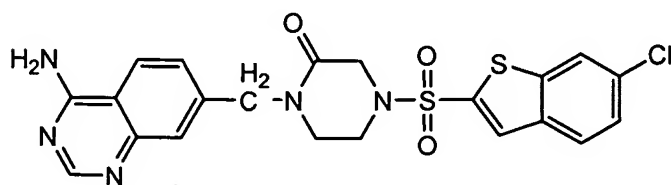
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A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

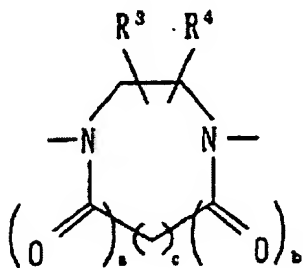
Claims 1, 2, 4, 9, 10, 17 and 23-26 are rejected under 35 U.S.C. 102(e) as being anticipated by United States Patent Application Publication 2004/0102450 (Ewing et al), which publication is based on a provisional application, number 60/072,707, which was filed 27 January 1998, almost seven months before applicants' earliest Japanese priority date.

Example 4, from the provisional application 60/072,707, upon which U.S. Patent Application Publication 2004/0102450 is based, discloses 1-(4-aminoquinazolin-7-ylmethyl)-4-(6-chlorobenzo[b]thiophene-2-sulfonyl)piperazin-2-one. The reference compound, whose structure is shown below, is described in Example 185 of the patent application publication:



1-(4-aminoquinazolin-7-ylmethyl)-4-(6-chlorobenzo[b]thiophene-2-sulfonyl)piperazin-2-one

Instant claim 1 embraces this compound when Q¹ represents a dicyclic fused ring group (4-aminoquinazoline); Q² is a single bond; T¹ is –CH(R¹³)– wherein R¹³ is hydrogen; Q³ is a group of the structure –



wherein R³ and R⁴ are both hydrogen, a is equal to 1 (one), b is equal to 0 (zero), c is equal to 2 (two); and Q^A is an unsaturated dicyclic fused ring group (6-chlorobenzo[b]thiophene).

The second alternative for Q^A set forth in claim 2 embraces the 6-benzothiophene group in the compound described in Example 185 of Ewing et al, wherein X³ is =C(R¹⁰⁰) where R¹⁰⁰ is hydrogen, X⁴ is sulfur atom, X⁵, X⁶, X⁷, X⁸ are all carbon atoms substituted with hydrogen.

Instant claim 9 is anticipated by Ewing et al because the piperazine ring in the compound of Example 185 thereof is embraced by the Q³ group shown above in the description of why instant claim 1 is anticipated by the reference compound.

Instant claim 10 is anticipated by Ewing et al because T¹ includes a methylene group, as provided for in the Example 185 compound from the reference.

A pharmaceutical composition according to instant claim 17 and methods of treatment according to instant claims 23-26 are disclosed in sections [2785] to [2801] of Ewing et al. Ewing et al's compounds are factor Xa inhibitors, like the compounds according to the present invention.

Conclusion

Any inquiry concerning this communication should be directed to Zachary Tucker whose telephone number is (571) 272-0677. The examiner can normally be reached Tuesday-Thursday from 8:00am to 4:30pm or Monday from 6:00am to 1:30pm. If Attempts to reach the examiner are unsuccessful, contact the examiner's supervisor, James O. Wilson, at (571) 272-0661.

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The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

zt

A handwritten signature in black ink, appearing to be "Z. Chen", written over the "zt" text.